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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/978,633	11/25/1997	ELAZAR RABBANI	ENZ-53	4639

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
02/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/978,633	RABBANI ET AL.	
	Examiner	Art Unit	
	J. E. Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/19/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *245-255,257-268,272-286 and 290-305* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *245-255,257-268,272-286 and 290-305* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/11/08, 1/12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 11/19/2007.

The amendment filed 11/19/2007 is acknowledged and has been entered.

Claims 245-255, 257-268, 272-286 and 290-305 are currently pending in the application and are addressed herein.

1. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on 1/11/2008 and 1/12/2008 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 245-255, 257-268, 272-286 290-303 and new claims 304, 305 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, essentially for the reasons of record as set forth in the 4/8/2003 Office Action.

Claims 263-265, 281-283, 299-301 and new claims 304, 305 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of selectively expressing a nucleic acid product in a cell in cell culture (in vitro), does not reasonably provide enablement for methods of expressing a nucleic acid product in a whole organism (in vivo). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, essentially for the reasons of record as set forth in the 4/8/2003 Office Action.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 247-248, 250-255, 257-259, 262-263, 266, 284 and 303 are rejected under 35 U.S.C. 102(e) as being anticipated by Meyer et al. (U.S. Patent 5,574,142), for the reasons of record set forth in the 4/8/2003 Office Action.

Response to Arguments

5. Applicant's arguments filed 10/10/2003 have been fully considered but they are not persuasive.

6. With respect to the written description rejection, Applicants argue that a representative number of species have been disclosed in the specification and figures.

In response, it is acknowledged that the specification does disclose several constructs, but the species disclosed are not sufficient to describe the entire genus of constructs encompassed by the claims. As previously indicated, the U1-antisense compounds are not considered representative of the genus of instantly claimed constructs which when present in a cell produce a product where said construct has at least one terminus comprising a polynucleotide tail hybridized to a complementary polynucleotide sequence and an antibody bound to said hybridized polynucleotide sequence, the construct being bound non-ionically to an entity comprising a chemical modification or a ligand. The U 1-antisense cassette vectors do not have noncovalent polymeric interactions. Even though they are composed entirely of polynucleotides in the form of a vector, the polynucleotide units in the Ul-cassette vectors are covalently bound to each other.

7. Applicants take issue with the assertion that the stick figures in the drawings do not adequately describe the chemical compositions. Applicants assert that figures 1-23 are sufficiently detailed and meet the criteria set forth in the MPEP. Applicants also submit 4 references which contain schematic diagrams for obtaining constructs and how they would function. Applicants also take issue with the assertion that it is necessary to

provide the chemical structure of the claimed nucleic acid compositions, antibodies or other components of the compositions that have the claimed functions in a cell. Applicants assert that this assertion is *contra* to the policies stated in the MPEP.

In response, it is respectfully pointed out that the issue is not with the way the figures are presented in schematic diagram. It is acknowledged that schematic diagrams are routinely used by those of skill in the art. The specific issue here is that the diagrams do not sufficiently describe the genus of molecules encompassed by the claims. In other words, the schematic diagrams (i.e. the "stick figures") in the drawings do not adequately describe the chemical compositions claimed to the extent that one of skill in the art would be able to readily envisage the administration of the claimed constructs to a cell for producing a product. For instance, one of skill in the art would not be able to readily recognize the genus of species encompassed by the claims based merely on the schematic drawings, which do not clearly demonstrate adequate description of the entire genus of species encompassed by the claims. As previously indicated, the specification as filed does not adequately describe a representative number of species of the claimed invention unless one of skill in the art would be able to envisage the structure, in this case the chemical structure (nucleic acid, protein, and other claimed chemical compositions, including the cells), of the claimed invention. Since none of the examples, either prophetic or exemplified by reduction to practice, in the specification as filed provide a clear description of the genus and species within the genus of the claimed invention, one of skill in the art would not have recognized that application was in possession of a representative number of species of the claimed invention at the time the invention was made.

Applicants contend that a detailed description of the compositions of the present invention are provided on pages 48-59 The terms "nucleic acid component", "domain", and "binder" are clearly defined on pages 48-49, and various examples of useful domains are described. Examples of various antibodies are provided in the paragraph bridging 53 and 54. These include useful domains with non-specific cell binding properties (see page 53), useful domains with specific cell binding properties (see page 53), useful domains with specific nucleic acid component binding properties (see page 54). Applicants also assert that the specification describes specific embodiments.

In response, these are not specific as they only provide general guidance as to what broad types of compositions are instantly claimed. The descriptions in both the specification and in the figures do not provide an adequate description of specific species, nor representative number of such species, of compositions which may be envisioned to produce a product in a cell, and have an antibody component, as claimed.

Wither respect to the enablement rejection, Applicants argue that various methods of for administering vectors into cultured cells and whole organisms and cite 4 references in support of their position (Yu, Miller, Ally, Lau). In response, the references have been considered but do not overcome the art-recognized problems previously indicated. For instance, delivery specifically to the target cells to reach the target site in the cytoplasm or nucleus and the ability to find and bind the target site and simultaneously avoid non-specific binding (see Branch and Ma).

Applicants also refer to 5 more post filing references in support of a correlation between in vitro and in vivo results.

Applicant is reminded that MPEP § 2164.01 indicates that the application, when filed, must contain sufficient information to enable one of skill in the art how to make and use the claimed invention. In other words, the claims must be enabled at the time of filing. Therefore, the post filing references do not demonstrate the instant claims were enabled for in vivo embodiments at the time the application was filed. In the instant case, in view of the art of record which demonstrates the unpredictability of the in vivo embodiments of the claims, the specification does not provide a disclosure which enables the full scope encompassed by the claims.

With respect to the rejection of claims under 35 USC 102(e), Applicants argue that Meyer **does not** contain all three elements in a single composition; therefore, the claims are not anticipated by Meyer et al.

In response, it is respectfully pointed out that the extracellular portion of Figure 2 teaches a non-natural entity which comprises at least one domain to a specific nucleic acid component (the antisense ODN), at least one domain to a cell of interest (the polymer carrier that interacts with the ASGP receptor), and said specific nucleic acid component (the antisense ODN). It is noted the claim does not indicate that the domain to a specific nucleic acid component and the specific nucleic acid component are required to be two different molecules. As such, the antisense ODN constitutes both the domain to a specific nucleic acid component and the specific nucleic acid component. Thus, Meyer does anticipate the instant claims.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635